

CLAIMS

We Claim

1. A set of oligonucleotide probes for detecting a plurality of different target polynucleotides, wherein a respective target polynucleotide corresponds to a single polynucleotide or a group of related polynucleotides, said set including a collection of different promiscuous probes, wherein a respective promiscuous probe is capable of hybridising to a target sequence shared between at least two of said target polynucleotides, wherein at least one target polynucleotide comprises at least two target sequences shared between other target polynucleotides, and wherein a predefined combination of promiscuous probes is capable of hybridising to said at least two target sequences, said predefined combination providing specificity of detection of said at least one target polynucleotide.
2. The set of probes of claim 1, comprising a plurality of different predefined combinations of probes, each providing specificity of detection of a different target polynucleotide.
3. The set of probes of claim 1, further comprising at least one non-promiscuous probe that is capable of hybridising to a unique target sequence of a single target polynucleotide.
4. The set of probes of claim 1, comprising at least one probe that is capable of hybridising to a pivot sequence, which divides two or more polynucleotides into distinct groups.
5. The set of probes of claim 1, comprising at least one degenerate oligonucleotide probe which is capable of hybridising to a redundant target sequence.
6. The set of probes of claim 1, wherein the probes are immobilised on a solid support.
7. The set of probes of claim 6, wherein the probes are in the form of a nucleic acid array.
8. The set of probes of claim 7, wherein the probes are in the form of a high-density nucleic acid array.

9. The set of probes of claim 6, wherein the probes are linked to the support via a spacer.

10. A method for detecting a plurality of different target polynucleotides using the set of probes of claim 1, said method comprising:

- exposing said probes to a test sample suspected of containing one or more of said target polynucleotides under stringent hybridisation conditions;
 - detecting which probes have hybridised to polynucleotides in said test sample;
- and
- processing the hybridisation data to determine which of said predefined combinations of probes has hybridised to said polynucleotides to thereby determine whether the test sample comprises any of said target polynucleotides.

11. The method of claim 10, wherein said stringent conditions favour high discrimination hybridisation.

12. The method of claim 10, further comprising analysing whether any of said target polynucleotides in said test sample corresponds to a phenotype-determining target polynucleotide.

13. The method of claim 12, further comprising diagnosing a phenotype of a patient from which said test sample was derived based on the phenotype-determining target polynucleotide(s) present in the test sample.

14. The method of claim 10, wherein said processing is performed by a programmable digital computer.

15. A method for detecting an unknown or uncharacterised member of a polynucleotide family using the set of probes of claim 1, said method comprising:

- exposing said probes to a test sample under stringent hybridisation conditions;
 - detecting which probes have hybridised to polynucleotides in said test sample;
- and
- processing the hybridisation data to determine which combinations of probes have hybridised to polynucleotides in said test sample, and whether any of said combinations is different to at least one predefined combination of probes that hybridise

to known target sequences, wherein the presence of a different combination of oligonucleotide probes is indicative of the presence of said unknown or uncharacterised member.

16. The method of claim 15, wherein the different combination of oligonucleotide probes corresponds to a hypothetical predefined combination of probes belonging to a predefined assemblage.

17. The method of claim 16, wherein the hypothetical predefined combination of probes comprises at least one degenerate oligonucleotide probe that is capable of hybridising to a redundant target sequence.

18. A process of identifying a set of target sequences from a plurality of known target polynucleotides for designing a set of oligonucleotide probes for detecting said target polynucleotides, wherein a respective target polynucleotide corresponds to a single polynucleotide or a group of related polynucleotides, said set including a collection of different promiscuous probes, wherein a respective promiscuous probe is capable of hybridising to a target sequence shared between at least two of said target polynucleotides, wherein at least one target polynucleotide comprises at least two target sequences shared between other target polynucleotides, and wherein a predefined combination of promiscuous probes is capable of hybridising to said at least two target sequences, said predefined combination providing specificity of detection of said at least one target polynucleotide, said process comprising:

- searching a nucleic acid sequence database comprising the sequences of said target polynucleotides for identical target sequences that are shared between two or more of said target polynucleotides to thereby obtain a subset of shared target sequences; and
- determining for each target polynucleotide a combination of target sequences from said subset which, when hybridised by complementary or substantially complementary oligonucleotide probes, facilitate specific detection of that target polynucleotide.

19. The process of claim 18, further comprising:

- determining a minimal or near minimal number of promiscuous oligonucleotide probes, which in different combinations, discriminate between the different target polynucleotides.

20. The process of claim 18, further comprising:
– sorting the target sequences from said subset to obtain a subset of pivot sequences which divide two or more polynucleotides into distinct groups.
21. The process of claim 18, further comprising:
– searching the database for sequences that are unique to respective target polynucleotides to thereby obtain a subset of unique target sequences;
– determining for each target polynucleotide a target sequence from said unique subset, or a combination of target sequences from said unique subset and said shared subset which, when hybridised by complementary or substantially complementary oligonucleotide probe(s), facilitate(s) specific detection of that target polynucleotide.
22. The process of claim 21, further comprising:
– determining a minimal or near minimal number of promiscuous probes which, in different combinations, together with one or more non-promiscuous probes, discriminate between the different target polynucleotides.
23. The process of claim 18, further comprising:
– searching the database for target sequences that are substantially identical or conserved between related target polynucleotides; and
– deducing redundant sequences corresponding to potential sequence variants of said target sequences to thereby obtain a subset of redundant target sequences which correspond to potentially unknown or uncharacterised target polynucleotides; and
– determining for each target polynucleotide a target sequence from said redundant subset, or a combination of target sequences from said shared subset and/or said redundant subset which, when hybridised by complementary or substantially complementary oligonucleotide probe(s), facilitate(s) specific detection of that target polynucleotide
24. The process of any one of claims 18, 20, 21 and 23, further comprising:
– sorting target sequences from said subset(s) to obtain target sequences with substantially similar affinities for their complementary or substantially complementary oligonucleotide probes.

25. A process of identifying a set of target sequences from a plurality of known target polynucleotides for designing a set of oligonucleotide probes for detecting said target polynucleotides, wherein a respective target polynucleotide corresponds to a single polynucleotide or a group of related polynucleotides, said set including a collection of different promiscuous probes, wherein a respective promiscuous probe is capable of hybridising to a target sequence shared between at least two of said target polynucleotides, wherein at least one target polynucleotide comprises at least two target sequences shared between other target polynucleotides, and wherein a predefined combination of promiscuous probes is capable of hybridising to said at least two target sequences, said predefined combination providing specificity of detection of said at least one target polynucleotide, said process comprising:

- searching a nucleic acid sequence database comprising the sequences of said target polynucleotides for identical target sequences that are shared between two or more of said target polynucleotides to thereby obtain a subset of shared target sequences;
- optionally searching the database for sequences that are unique to respective target polynucleotides to thereby obtain a subset of unique target sequences;
- searching the database for target sequences that are substantially identical or conserved between related target polynucleotides and deducing redundant sequences corresponding to potential sequence variants of said target sequences to thereby obtain a subset of redundant target sequences which correspond to potentially unknown or uncharacterised target polynucleotides.
- determining for each target polynucleotide a target sequence from said unique subset or from said redundant subset, or a combination of target sequences from said shared subset and/or from said redundant subset which, when hybridised by complementary or substantially complementary oligonucleotide probe(s), facilitate specific detection of that target polynucleotide.

26. The process of claim 25, further comprising:

- sorting the target sequences from said redundant subset, from said shared subset and, if any, from said unique subset to obtain target sequences with substantially similar affinities for their complementary or substantially complementary oligonucleotide probes.

27. The process of claim 25, further comprising:

—determining a minimal or near minimal number of promiscuous probes which, in different combinations, together with one or more non-promiscuous probes, discriminate between the different target polynucleotides.

28. The process of claim 18 or claim 25, wherein said process is performed by a digital computer.

29. A computer program product for identifying a set of target sequences for designing a set of oligonucleotide probes according to claim 1, comprising code that receives as input sequences of target polynucleotides in one or more nucleic acid sequence databases and/or information that identifies sequences corresponding to said target polynucleotides; code that identifies potential target sequences within the target polynucleotides; code that creates a database that registers the presence or absence of possible target sequences found within respective target polynucleotides; code that identifies the target sequences that are shared between different target polynucleotides; optional code that identifies the target sequences that are unique to specific target polynucleotides, code that assesses every possible combination or a number of combinations of the target sequences to identify those combinations of target sequences which, when hybridised to complementary oligonucleotide probes, will facilitate discrimination between different target polynucleotides; and a computer readable medium that stores the codes.

30. The computer program product of claim 29, further comprising code that identifies substantially identical or conserved sequences between the target sequences and code that identifies redundant sequence variants of said substantially identical target sequences, wherein said redundant sequence variants are registered as target sequences.

31. A computer program product for processing hybridisation data using the set of oligonucleotide probes according to claim 1, comprising code that identifies for each target polynucleotide a combination of features in an oligonucleotide array whose probes facilitate specific detection of that polynucleotide; code that receives as input hybridisation data from hybridisation reactions between sample polynucleotides and the oligonucleotide probes in the array; code that processes the hybridisation data to determine whether the sample polynucleotides comprise any of the target polynucleotides by searching for hybridisation

patterns that match any of the predefined combinations or predefined assemblages of target sequences; and a computer readable medium that stores the codes.

32. The computer program product of claim 31, further comprising code that receives as input the sequence of an oligonucleotide probe in each feature of an oligonucleotide array and code that receives as input a database that contains information on the presence or absence of target sequences in target polynucleotides.

33. The computer program product of claim 31, further comprising code that deduces the probability that the detected pattern of hybridisation indicates the presence of a target polynucleotide.

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